Seasonal Distribution of Poliomyelitis*

CHARLES ARMSTRONG, M.D., F.A.P.H.A.

Medical Director, U. S. Public Health Service, Microbiological Institute, National Institutes of Health, Bethesda, Md.

THERE are certain epidemiological features of poliomyelitis which have been so frequently and so generally observed that they are recognized as characteristics of the disease. One such characteristic is a tendency for the seasonal variation of poliomyelitis to be slight in the tropics, with a tendency for outbreaks to be confined to the warm months of the year as one proceeds either north or south from the equator. It is this epidemiological feature of the disease which will be here discussed, not with a view to explaining minute variations or exceptional occurrences but from a rather broad viewpoint, i.e., to observe the forest rather than the individual trees.

Means of Transmission — Any discussion of the seasonal incidence of a disease must consider the method of transmission. Contact, arthropods, food, and water are all recognized as possible means for the transmission of poliomyelitis. The space allotted for this discussion will not, however, permit a detailed consideration of available evidence bearing on these several possibilities. While it must be admitted that occasional cases may be acquired by each of these methods, the evidence, at least to my mind, is overwhelming in indicating contact as the one common means of transmission, especially such close personal contacts as occur within a household.

We are therefore confronted with the difficulty of explaining why poliomyelitis, a disease transmitted by close contact, should be most prevalent in that portion of the year when people spend most of their time in the open and why it should tend to wane rapidly when cool weather induces people to congregate indoors in search of warmth, a behavior quite in contrast to other contagious diseases such as diphtheria, measles, etc. Several theories have been suggested in an effort to explain this anomaly of poliomyelitis outbreaks:

1. Poliomyelitis virus has been assumed to be capable, in warm weather, of multiplication outside susceptible human cells, possibly in fecal bacteria, Franconia and Zellweger 1942,[1] or in water protozoa, Kling, Olin, Fahraeus and Norin 1943,[2] or that the virus is a filterable phase of the streptococcus, Rosenow 1944.[3] The failure to demonstrate multiplication in such organisms was explained by Gard (1943)[4] by assuming that a mutation from an inactive intestinal virus to an active central nervous system virus occurred along the way. Not only is direct proof of these assumptions lacking, but on this theory the increased summer incidence would probably be food—or water-borne which is not compatible with the epidemiology of poliomyelitis.

There is considerably more circumstantial evidence tending to incriminate certain filth-associated arthropods as transmitters of the disease. There are, however, certain factors which are incompatible with this assumption, for instance: (a) the world-wide distribu-

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tion of the disease, (b) the failure of poliomyelitis to lessen in cities where flies have been greatly depleted over the years by the elimination of horses and the installation of modern sewerage systems, (c) the immunological pattern of the disease in the population, and (d) the occurrence of winter outbreaks.

2. A second theory is that of Aycock 1930,[5] who attributes the summer incidence to an assumed lowering of resistance due to failure of the human defense mechanism to adjust itself to the sudden change from a cool to a warm season, especially when the temperature variation tends to be great. Peterson in 1942 [6] proposed a similar theory and attributed the lack of resistance in late summer and fall to a diminishing duration of daily sunshine, which reduction begins in the northern hemisphere about June 21 and in the southern in December. These assumptions of Aycock and of Peterson are more in accord with epidemiological evidence because they assume infection to be by contact; however, no variations in host susceptibility to, or infectivity of the virus sufficient to account for the seasonal incidence in man have been observed in experimental studies. Furthermore, these hypotheses leave us with the difficulty of explaining why so fundamental a mechanism as that of resistance to disease should behave seasonally in poliomyelitis in one way and with most other contact diseases in another. Especially does this appear difficult in view of recent developments which have tended to bring the immunological behavior of poliomyelitis into line with that of other contact diseases.

3. There is, however, a third possibility, namely, that the usual portal of effective entrance for the virus of poliomyelitis in man may tend to be more permeable during warm weather than in cold. It is this possible explanation for the seasonal variation of poliomyelitis which will be here considered.

Portal of Entrance and Seasonal Incidence of Poliomyelitis — The assumption that the seasonal incidence of poliomyelitis depends upon variations in the permeability of the usual portal of entry for the virus does not require the assumption of any extra human source of multiplication for the virus or of any seasonal alteration in the basic resistance of the population, or any seasonal variation in the infectivity of the virus. It does, on the other hand, relate the observed seasonal variation to an external mechanism more directly in contact with variable seasonal factors of our environment — factors which are capable of producing observable alterations. For instance, it is a rather general experience that nasal and throat secretions tend to be more copious in cool weather after fires have been started than is the case in warmer portions of the year and upper respiratory infections tend to be more prevalent. Let us therefore consider the nasal secretions.

Specific Antibodies in Nasopharyngeal Secretions—Amoss and Taylor (1917),[7] Howitt (1937),[8] and Bell (1948),[9] demonstrated the presence of specific antibodies against poliomyelitis virus in the nasal secretions of a portion of the persons examined, and the latter two authors demonstrated that the content of antibodies in the secretions tended to vary with the content of antibodies in the serum, but at a lower level. We have recently demonstrated that nasal washings taken on the same individual when the mucous membranes were quiescent, and when stimulated to secretion by an experimentally induced upper respiratory inoculation, showed a higher content of antibodies in the latter washing,[10] indicating that the antibody content persisted with the induced secretion and was not simply diluted by it. In winter, the breathing of cool air of low humidity would tend to con-

centrate existing secretions through drying. Thus, it is conceivable that some persons who might upon exposure become victims or carriers of the virus in summer would tend to spread no virus or a neutralized one in winter.

The problem which we are considering, however, would appear to be largely concerned with persons in whom specific antibodies are lacking.

Nasopharyngeal Secretions of Non-Immune Persons—The normal mucous secretions long have been considered to be a protective mechanism Florey,[11] and are present throughout the respiratory and alimentary tracts. Considering either location as a possible portal of entry, the upper respiratory tract appears to be more directly exposed to climatic variations than is the alimentary tract. To this extent, the concept under consideration would appear to favor the nasopharynx as the more probable portal of entry and of exit for the virus effective in the spread of poliomyelitis. This possibility is supported by the fact that the virus has been frequently demonstrated in the throat for a few days before to a few days after onset of symptoms, a period which has, on epidemiological grounds, come to be considered as the infectious period of the disease.[12-16, etc.]

The occurrence of poliomyelitis following tonsillectomy,[17-21] and certain experimental evidence also support the nasopharynx[22, 23] as a possible portal of entry for the virus.

Nonspecific Action of Mucin—Nungester, Wolf, and Jourdonnais (1939)[25] demonstrated that certain bacteria, harmless to experimental animals, when injected intraperitoneally in ordinary diluents became rapidly lethal when 5 per cent of gastric mucin was incorporated with the same dose of organisms.

Various explanations for this observed fact have been suggested, the simplest of which is that mucin acts by coating the bacterial cells and possibly the peritoneal cells as well, so that the organisms are protected from the animal's cellular and perhaps other defense mechanisms while remaining in an environment suitable for their multiplication.

Now, if this simple explanation be wholly or in part correct for bacteria, it appears that the effect might be reversed in case of a virus, which must come in close contact with and enter a susceptible cell before multiplication can occur. The avidity with which a mucin containing solution clings to dry glassware and its facility for plugging siliceous filters suggests that mucin might hold in addition an attraction for negatively-charged virus particles.

Certain it is that poliomelitis reaches its highest incidence in temperate climates when upper respiratory infections are at their lowest ebb and secretions from the membranes are tending toward a minimum. Whether the nasopharyngeal secretions have any such action as suggested or not, the presence of an abundant secretion on a surface would certainly tend to dilute and to carry away any accompanying virus.

Let us now consider the upper respiratory passages when such natural irritants as cold, drying or upper respiratory infections tend to stimulate secretions.* In cold weather the atmosphere, whether warmed artificially or by inspiration, suffers a drop in relative humidity with a corresponding tendency to take up moisture and thus to stimulate normal membranes to additional secretion, which secretions tend to be concentrated through drying while common upper respiratory infections show a tendency to develop.

In warm weather the temperature of the atmosphere and its relative humidity are less altered by inspiration

* It has been demonstrated that mucous secretions are stimulated by locally acting irritants rather than by nerve inpulses (Florey[26]).

and as commonly observed, upper respiratory secretions and common infections are at a minimum while poliomyelitis tends to reach its greatest prevalence.

Atmospheric temperature in cold weather is far more subject to artificial regulation than is humidity; therefore, it might seem possible that under actual conditions of living as in the United States, atmospheric humidity is more important in influencing susceptibility to exposure than is temperature.

There is, however, a striking correlation between seasonal (summer) temperatures and the occurrence of poliomyelitis as noted in temperate climates; the correlation with atmospheric humidity is, however, less apparent. In so far as atmospheric variations may directly affect the respiratory membranes, it is evident that it is the conditions of the air within the respiratory tract and not at some weather station, that are of significance. We must, therefore, take into consideration the effect of warming the atmospheric air to the temperature of air within the respiratory passages. The expired air is always at a temperature of about 90° F. and 90 per cent saturated with moisture. It is therefore the difference between the absolute humidity of inspired air and the absolute humidity of 90 per cent saturated air at about 90° which measures drying effects on the mucous membranes. A striking correlation between absolute humidity and the incidence of poliomyelitis is clearly apparent.

Relative Humidity of Inspired Air at a Given Temperature — Through the courtesy of Dr. W. D. Woods of the U. S. Weather Bureau, tables showing the average monthly temperature and relative humidity were secured for Washington, D. C., during 1949.

From these data it was possible to

FIGURE 1

AVERAGE MONTHLY ATMOSPHERIC TEMPERATURE, AVERAGE MONTHLY RELATIVE HUMIDITY AT ATMOSPHERIC TEMPERATURE (7 AM.) AND ATMOSPHERIC RELATIVE HUMIDITY ADJUSTED TO TEMPERATURE OF 88° F., AND POLIOMYELITIS CASES BY MONTH OF ONSET WASHINGTON, D. C., 1949

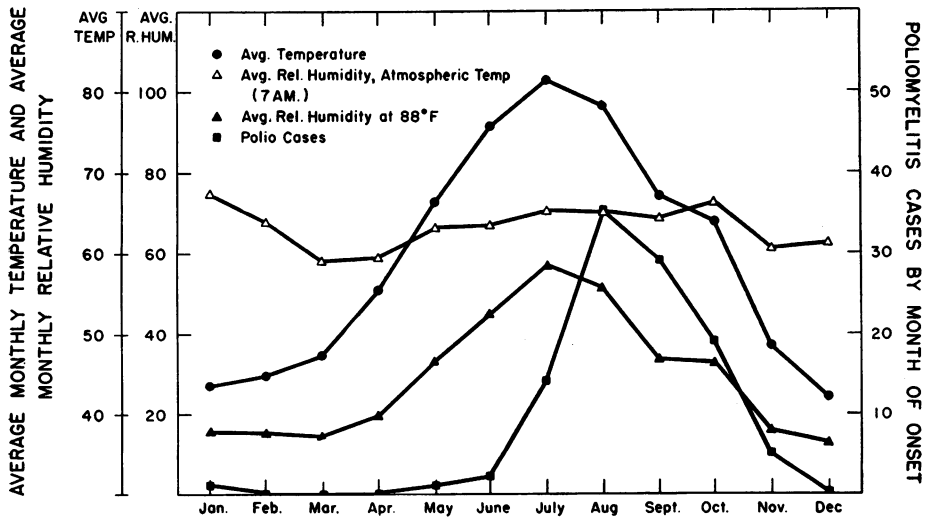
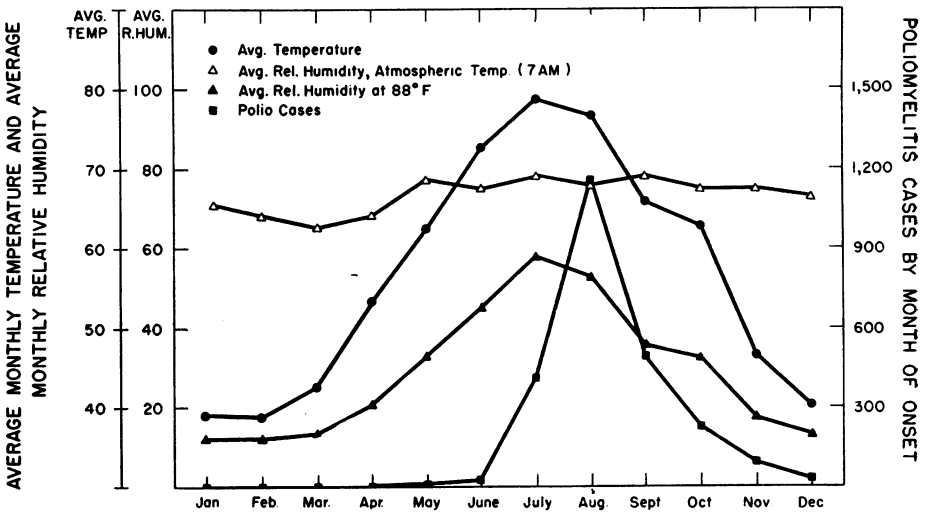


FIGURE 2

AVERAGE MONTHLY ATMOSPHERIC TEMPERATURE, AVERAGE MONTHLY RELATIVE HUMIDITY AT ATMOSPHERIC TEMPERATURE (7 AM.) AND ATMOSPHERIC RELATIVE HUMIDITY ADJUSTED TO TEMPERATURE OF 88° F., AND POLIOMYELITIS CASES BY MONTH OF ONSET NEW YORK CITY, 1949



determine the relative humidity of the atmosphere at any assumed temperature (which is, of course, the equivalent of absolute humidity). In Figure 1 is shown the relative humidity of the atmosphere and of the same air when warmed, as through inspiration, to an assumed temperature of 88° F.* Figure 1 also records the reported cases of poliomyelitis for Washington by month of onset for the same year. The similarity of the latter two curves is striking.

The same type of data for New York City 1949 are shown in Figure 2. Again a similarity between the curve of relative humidity at 88° F.* and for the monthly incidence of poliomyelitis is apparent.

Susceptibility to Infection — Our concept attempts to relate the summer prevalance of poliomyelitis, the development of immunity, and the regeneration of virus to the conditions which prevail at a portal of entrance and of exit for the virus, but it has nothing to do with whether effectively exposed non-immune individuals develop recognizable symptoms or simply immunity—such considerations being related to natural resistance as it relates to age, sex, overexertion, and perhaps other factors rather than to the permeability of a portal of entry.

If this simple concept is operative, it is necessary, however, to assume that it acts differently in poliomyelitis from in measles, mumps, chickenpox, smallpox, or influenza which tend toward a cool weather prevalence. This difference does not appear entirely illogical, however, since poliomyelitis virus induces recognizable symptoms by reaching susceptible cells of the central nervous system by way of nerve fibers and tracts and has no demonstrated attraction for surface cells and no demonstrated

* Other temperatures above the monthly average could have been selected without markedly altering the shape of the curve except that it would tend to be raised or lowered.

synergistic action with bacteria. The other viruses mentioned, however, are capable of parasitizing surface cells and have in some instances an attraction for certain available cells as revealed by the red cell agglutination phenomenon or a possible synergistic action with some types of the varying but ever present bacterial flora of the respiratory tract. Under such circumstances, it appears possible that the opportunities for infection to pass from one person to the next are more important in the case of those infections showing winter prevalence than are the local conditions at the virus implanted area. If the concept under consideration is, however, effective in poliomyelitis, we should expect the closer person-to-person contacts of winter to be relatively ineffective due to the relatively greater scarcity of virus during the cool portions of the year.

We have thus far stressed the possible effect of atmospheric conditions upon the nasal mucous membranes and their secretions and said very little concerning the possible effects of common upper respiratory infections which lead to cellular changes as well as to markedly increased secretions.

There is, in so far as I am aware, little direct evidence on this point, although local responses to infection are generally considered to be defensive in nature and there is indication that certain bacteria or their products may exert a hindering effect upon certain virus infections such as vaccinia,[21, 28] and mouse pneumonia.[29]

Recently a number of therapeutic agents have come into common use in the United States which exert an inhibitory effect upon several types of organisms commonly present in the upper respiratory passages. It is therefore interesting to speculate upon the possible relationship of their employment to the high incidence of poliomyelitis reported in the United States for 1948–1949 and 1950 to date.

The usual and apparently logical explanation for this situation is that it is due to the more frequent reporting of mild illnesses as poliomyelitis. This could readily explain why deaths have not risen in number as have the reported cases; however, this explanation is not conclusive since we are ignorant as to what has been accomplished, if anything, either in the treatment or prevention of the fatal types of poliomyelitis. We therefore at this time can do little more than raise the question for future study.

Experimental Evidence — In so far as the mucuous secretions are concerned, apart from any underlying cellular response, it appears that it should be possible to test experimentally some of the suggestions offered earlier as deductions.

For instance, does gastric mucin tend to snare virus particles? Tubes containing a uniform amount of poliomyelitis virus (Lansing strain) with varying amounts of mucin (0.8, 1.6, and 3.0 per cent) in buffered saline pH 7.6 and a control tube with no mucin present were centrifuged at 13,000 r.p.m. for 30 minutes, the insoluble portion of the mucin appearing to be completely sedimented. The supernatant fluid from each tube was then inoculated intracerebrally into white mice. Table 1, test 143, indicates that supernatant fluid from the tube which contained the highest concentration of mucin was least infectious. Supernatant from control tubes containing no mucin was more potent. A similar experiment was made employing herpes simplex virus with and without mucin centrifuged at 8,000 r.p.m. for 15 minutes. The results were similar to those above (Table 1, test 168).

Next, an attempt was made to see if mucin in the presence of herpes simplex virus would delay or prevent its lethal effects as compared with the same

TABLE 1

EFFECT OF CENTRIFUGATION UPON VIRUS SUSPENSIONS WITH AND WITHOUT MUCIN

TEST NO.	VIRUS	PERCENT MUCIN	ROUTE INOC.	NO. MICE INOC.	NO. MICE DEAD OF INFECTION	NO. MICE SURVIVING
143	Polio.	0.8	I. C.	12	10	2
		1.6	I. C.	12	12	0
		3.0	I. C.	12	6	6
		0	I. C.	12	12	0
168	Herpes Simplex.	0.55	I. C.	12	1	11
		1.1	I. C.	12	1	11
		0	I. C.	12	11	1
		1.1*	I. C.	12	12	0

I. C. = Intracerebral.

* This dose of virus added to supernatant following centrifugation to control effect of any soluble mucin in supernatant.

amount of virus in the same diluent without mucin, when inoculated intracerebrally into white mice. The results shown in Table 2, tests 134, 135, and 139, indicate that gastric mucin does tend to delay the death of the animals as compared with the controls and that 4 out of 30 mice which received herpes virus in mucin intracerebrally recovered while none of 43 controls survived. The animals inoculated with the virus mucin mixtures were somewhat depressed for 24 hours and it is conceivable that the reaction thus engendered played a part in the results. Mice dying within 24 hours of inoculation were discarded. Next, the effect of mucin upon herpes simplex infection of mice inoculated into the pad of the right hind foot was investigated. The results as shown in Table 2, test 161, reveal a similar significant prolongation of life and reduction in the number of deaths among mice receiving the virus plus mucin as compared to the controls.

Inoculations (0.1 ml.) into the pad of the foot develop considerable pressure and it was therefore felt that inocula-

TABLE 2

EFFECT OF GASTRIC MUCIN ADDED TO VIRUS AS REVEALED BY DEATHS OF INOCULATED MICE.

TEST NO.	VIRUS	VIRUS IN	ROUTE INOC.	REJ	DEATHS BY DAYS																					AVG. DAYS LIFE	SURVIVED INOC.
					2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24		
134	Herpes	S	IC.				2	4																				4 2/3	0/6
		S + M	IC.			1			2	1	1																6 1/5	1/6
135	"	S	IC.				1		3	2																	6	0/6
		S + M	IC.	1					-	1						1											10	3/5
139	"	S	IC.	1		1	6	3	1																		4 4/11	0/11
		S + M	IC.	4				5	1	1	1																5 3/4	0/8
161	"	B	Pad								1	2	3	6	3	1	3					1	1				12	4/25
		B + M	"												2		1	4		1			1			1	15 9/10	15/25
162	"	B	Groin										4	2	1	1	2				1						12 1/11	14/25
		B + M	"											1													11	24/25
164	Rabies	S	IC.				2		1	3	4	2															7 1/12	0/12
		S + M	IC.							3	3			1													8	5/12
163	"	S	IM.								2	4	3														9 1/9	3/12
		S + M	IM.										1														10	11/12

S = Saline M = Mucin 3 to 4 % B = Broth IC. = Intracerebrally IM. = Intramuscularly REJ = Rejected

tions into a loose tissue might simulate the conditions of a natural surface infection more closely. Twice the quantity of inoculum employed in the pad was therefor injected into the loose tissue of the groin in two groups of mice. Only 1 of 25 mice receiving the virus plus mucin succumbed while 11 of 25 receiving the same dose of virus in the same menstruum but without mucin died (Table 2, test 162).

Next, tests were carried out with and without mucin, employing the Gochenauer strain of rabies virus inoculated both intracerebrally and by intramuscular routes (Table 2, tests 164 and 163). The results were similar to those already cited and since rabid animals uniformly die the results distinctly indicate a preventive action by the mucin. All mice were observed for at least 3 weeks. Immunity tests on surviving mice have not yet been made. Herpes simplex and rabies virus were substituted for poliomyelitis in the above tests in order to escape the very variable incubation period observed with the Lansing strain of poliomyelitis in mice and because the Lansing virus is not pathogenic for mice by other than intercerebral routes. The mucin employed was granular mucin, type 1701-W, manufactured by the Wilson Laboratories, Chicago.

It is conceivable that this protective effect might have been even more impressive had it been possible to provide a continuous supply of fresh mucin, as would appear possible upon a mucin-secreting surface membrane, and had it been possible for excess mucin to have escaped from the inoculation site.

Accord with Experience — The suggested hypothesis appears to accord with seasonal behavior of poliomyelitis such as:

1. The behavior of poliomyelitis in the tropics.
2. The variations that occur in the incidence curves in different latitudes, for instance, the tendency for the earlier onset and later regression of poliomyelitis in the Southern United States as compared to northern areas.
3. The fact that in World War II American soldiers in the tropical orient suffered notably from poliomyelitis,[30,31] while in World War I our troops, likewise subject to exposure to troops from many lands, were practically free from the disease, notwithstanding the more rigorous climate of France and the severe exposure of trench warfare.
4. This hypothesis would appear elastic enough to permit of the exceptional seasonal incidence occasionally encountered, such as the shift of the peak incidence from one month to another in different outbreaks of the same locality as in New York 1916–1931, or the occurrence of an occasional cold weather outbreak which would be quite incompatible with transmission by any arthropod now recognized as a possible transmitter of the virus.

Bearing of Hypothesis on Control — If seasonal incidence of poliomyelitis is related, as suggested, to the conditions of a portal of entry or of exit for the virus effective in the spread of the disease, it is conceivable that such conditions might be susceptible to alterations through artificial measures which would tend to hinder effective exposure.

However, since such measures would not appear capable of influencing susceptibility once effective exposure had occurred, but might simply tend to defer infection to a later and more susceptible age period, the desirability of such procedures would at this instant appear questionable, unless it can be demonstrated that exposure under such modified conditions tends to result in specific immunization in the absence of serious infection.

At least, the concept suggests numerous lines for epidemiological and laboratory investigation, which, it is hoped may elucidate the mechanism and help to remove the mystery surrounding a baffling characteristic of poliomyelitis outbreaks.

SUMMARY AND CONCLUSION

In an attempt to explain the seasonal incidence of epidemic poliomyelitis, a

hypothesis is suggested which requires no assumptions of an extra human source or change of infectivity for the virus nor any assumed alteration in the susceptibility of the population to infection. On the other hand, it attempts to relate the seasonal behavior of poliomyelitis to generally observed alterations in the upper respiratory tract due to atmospheric changes, notably in temperature and relative humidity of inspired air. The upper respiratory passages are viewed not only as a portal of entry for the virus but also as a portal of exit for the virus most effective in transmitting the diseases from person to person.

REFERENCES

1. Franconi, G., and Zellweger, H. Zur epidemiologic der Kinderlahmung. *Schweiz. med. Wchnschr.* 1942, p. 1025.
2. Kling, C. A., Olin, G., Fahraens, J., and Norlin, G. Sewage as a Carrier and Disseminator of Poliomvelitis Virus. *Acta med. Scandinav.* 112:217–250, 1942.
3. Rosenow, E. C. Production of a Filterable Agent from Alpha Streptococci. *Am. J. Clin. Path.* 14:150, 1944.
4. Gard, S. Microscopic Observations on Purified Preparations of Poliomyelitis Virus; a Contribution to the Question of the Epidemiology of Infantile Paralysis. *Klin. Wchnschr.* 22:315, 1943.
5. Aycock, W. L. Seasonal and Age Studies on Poliomyelitis and What They Suggest. *A.J.P.H.* 20:41, 1930.
6. Petersen, H. The Relation between Light and the Epidemic Curve of Poliomyelitis with an Attempted Epidemic Theory Explaining Epidemic Waves as a Statistical Consequence of the Mechanism of Infection. *Acta med. Scandinav.* 107:282, 1941.
7. Amoss, H. L., and Taylor, H. Neutralization of the Virus of Poliomyelitis by Nasal Washings. *J. Exper. Med.* 25:507, 1917.
8. Howitt, B. F. Relationship between Nasal and Humoral Antipoliomyelitis Substances. *J. Infect. Dis.* 60:113, 1937.
9. Bell, E. J. The Relationship between the Antipoliomyelitis Properties of Human Nasopharyngeal Secretions and Blood Serums. *Am. J. Hyg.* 47: 315, 1948.
10. Armstrong, Charles, and Atlas, L. T. Unpublished data.
11. Florey, H. L. Observations on the Function of Mucous and the Early Stages of Bacterial Invasion of the Intestinal Mucosa. *J. Path. & Bact.* 37:283–289, 1933.
12. Taylor, E., and Amoss, H. L. Carriage of the Virus of Poliomyelitis with Subsequent Development of Infection. *J. Exper. Med.* 26:745, 1917.
13. Vignac, A. J., Paul, J. R., and Trask, J. D. The Recovery of the Virus of Poliomyelitis from Extra Neural Sources in Man with a Survey of the Literature. *Yale J. Biol. & Med.* 11, 15–31, 1938.
14. Kramer, S. D., Hoskwith, B., and Grossman, L. H. Detection of Virus of Poliomyelitis in the Nose and Throat and Gastrointestinal Tract of Human Beings and Monkeys. *J. Exper. Med.* 69:49–67, 1939.
15. Howe, H. A., and Bodian, D. Isolation of Poliomyelitis Virus from the Throat of Symptomless Children. *Am. J. Hyg.* 45:219–222, 1947.
16. Casey, A. E., Fishbein, W. I., Schabel, F. M., and Smith, H. T. Epidemiologic Implications of Poliomyelitis Virus in the Throat. *South. M. J.* 42: 427–429, 1949.
17. Aycock, W. L., and Luther, E. H. The Occurrence of Poliomyelitis following Tonsillectomy. *New England J. Med.* 200:1164, 1929.
18. Carey, W. Poliomyelitis following Tonsillectomy. *J. Iowa Med. Soc.* 32:259, 1942.
19. Toomey, J. A., and Krill, C. E. Tonsillectomy and Poliomyelitis. *Ohio State M. J.* 38:653, 1942.
20. Howard, R. E. Relationship of Poliomyelitis and Tonsillectomy. *Am. Otol. Rhin. & Laryng.* 53: 15, 1944.
21. Visquez H. J. Tonsillectomy and Heine-Medin Disease. *Arch. argent. de pediat.* 21:548, 1944, and 22:266, 1944.
22. Kling, C., Levaditi, C., and Hormus, G. Comparison between the Different Modes of Contamination of Monkeys by Poliomyelitis Virus. *Bull. Acad. de med., Paris* 111:709, 1934.
23. Faber, H. K., Silverberg, R. J., and Dong, L. Poliomyelitis in Cynamolgous Monkeys; Comparison of Upper Portion of Alimentary Tract with Its Lower Gastrointestinal Portion as a Port of Entry, with Special Reference to Peripheral Ganglia. *J. Exper. Med.* 788:499, 1943.
24. Faber, H. K., Silverberg, R. J., and Dong, L. Poliomyelitis in Cynamolgous Monkeys; Infection by Inhalation of Droplet Nuclei and Nasopharyngeal Portal of Entry, with Note on This Mode of Infection in Rhesus. *J. Exper. Med.* 80:39, 1944.
25. Nungester, W. J., Jourdonnais, L. F., and Wolf, A. A. Effect of Mucin in Infections by Bacteria. *J. Infect. Dis.* 59:11–21, 1936.
26. Florey, H. L. The Secretion of Mucin by the Colon. *Brit. J. Exper. Path.* 11:348, 1930.
27. Armstrong, Charles. Modification of the Vaccine Response in Rabbits by the Application of Diphtheria Toxin to the Vaccination Site. *Pub. Health Rep.* 48:17, 1933.
28. Armstrong, Charles. Unpublished data.
29. Landy, M., and Batson, H. C. On the Identity of the Virulence Enhancement Factor in Gastric Mucin. *J. Immunol.* 62:477, 1944.
30. Paul, J. R., Havens, W. P., and Van Rooyen, C. E. Poliomyelitis in British American Troops in the Middle East. The Isolation of Virus from Human Feces. *Brit. M. J.* 1, 841–843, 1944.
31. Paul, J. R. Poliomyelitis Attack Rates in American Troops 1940–1948. *Am. J. Hyg.* 50–57, 1949.